

### Remarks

Claims 163, 165, 171, 175, 176, 179, 183, 193 and 196 are amended herein. New claims 211-234 are added herein. Upon entry of this amendment, claims 163-209 and 211-234 will be pending.

### Amendments to the Specification

Applicants hereby amend the specification to include consistency paragraphs directed to the amended claims. The addition of such paragraphs does not constitute an addition of new matter.

### Supplemental Information Disclosure Statement

A Fifth Supplemental Information Disclosure Statement is submitted herewith. Applicants respectfully request review and entry of the cited references.

### Objections under 37 C.F.R. § 1.75

Reconsideration of the objection of claims 193-196 under 37 C.F.R. § 1.75 as being duplicates of claims 171, 172, 174, and 175 is respectfully requested.

The M.P.E.P. states that a duplicate claim objection is proper if (i) "two claims in an application are duplicates" or (ii) "are so close in content that they both cover the same thing, despite a slight difference in wording."<sup>1</sup> But beyond these two categories, the M.P.E.P. concedes that "court decisions have confirmed applicant's right to restate (i.e., by plural claiming) the invention in a reasonable number of ways. Indeed, **a mere difference in scope** between claims has been held to be enough."<sup>2</sup>

The claims in question do not fall within the two duplicate-claim categories set forth in the M.P.E.P. They are not exact duplicates of one another, and they are not so close in content that they both cover the same thing. All of the claims at issue define plastic stirrers, and claim 193 defines couplings "for releasably connecting the plastic stirrers to the drive system." But claim 171 goes further than claim 193, defining "**metal spindle portions** associated with the

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<sup>1</sup> M.P.E.P. § 706.03(k).

vessels **[and] couplings** on the metal spindle portions for releasably coupling the plastic stirrer to the metal spindle portion for rotation therewith." By defining both "metal spindle portions" and "couplings," claim 171 clearly meets the criteria set forth above of establishing "a mere difference in scope between claims." As such, claims 193-196 are not duplicates of claims 171, 172, 174, and 175 because they do not include "metal spindle portions."

### **Rejections under 35 U.S.C. §103**

#### **Claim 163**

Reconsideration of the rejection of claim 163 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Amended claim 163 defines a parallel reactor having vessels for containing the reaction mixtures and multi-piece spindles for stirring the reaction mixtures in the vessels. Each multi-piece spindle comprises (a) a metal upper spindle portion, (b) a **single use plastic stirrer comprising a shaft having a plastic core** and a plastic mixing blade on the shaft, and (c) a coupling for releasably coupling the plastic stirrer to the metal upper spindle portion in a position wherein the stirrer extends down into a respective vessel. In addition, amended claim 163 states that each plastic stirrer is **removable from the coupling after a mixing operation to permit discard and replacement of the stirrer after a single use.**

Nelles and the other references of record fail to disclose these novel features. In brief, Nelles discloses a mandrel (ruhrerwelle) extending from near the bottom of the vessel to a coupling (kupplung) well outside the confines of the vessel.<sup>3</sup> Nelles' mandrel design fails to show or suggest a multi-piece spindle having both a metal upper spindle portion and a single use plastic stirrer. Nelles also fails to disclose a **single use plastic stirrer with a shaft having a plastic core removable from the coupling after a mixing operation to permit discard and replacement of the stirrer after a single use.** Lebl discloses no single use plastic stirrer comprising a shaft having a plastic core to permit discard and replacement of the stirrer after a single use, and Corkan merely discloses stir bars. Moreover, Salvat does not teach or suggest a **single use plastic stirrer**

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<sup>2</sup> *Id.* (emphasis added).

removable from the coupling after a mixing operation to permit discard and replacement of the stirrer after a single use. Finally, Aldrich discloses no stir shafts having a plastic core, and no single use plastic stirrers permitting discard and replacement of the stirrers after a single use. As a result, the aforementioned cited references cannot render claim 163 obvious.

With respect to the newly cited references Salzman and Strah, they too lack adequate teaching to render amended claim 163 obvious. In particular, the Salzman reference cited by the Examiner (hereinafter Salzman '91) teaches replacement of traditionally metallic mixing components (e.g., impellers, shafts, housings and drive elements) with fiber-reinforced plastics.<sup>4</sup> Salzman '91 teaches that plastics without fiber-reinforcement have traditionally been used in other applications in the chemical process industry (e.g., vessels, scrubbers, hoppers, hoods, ducts, etc.).<sup>5</sup> Salzman '91 teaches that the adoption of such plastics for fluid mixers, however, lags behind because of the high dynamic loads to which such mixers are subjected. To provide mixers capable of withstanding such high dynamic loads, Salzman '91 teaches the use of fiber-reinforced plastics.<sup>6</sup> Because the mechanical properties of such materials are anisotropic, Salzman '91 further teaches that simply adding fibers to plastic is not enough; rather, the reinforcing fibers must be precisely arranged within the plastic depending upon the load requirements of the mixer.<sup>7</sup> In particular, Salzman '91 discloses hand lay-up, compression molding and resin-transfer molding as preferred formation techniques for larger impellers, up to 134 inches in diameter.<sup>8</sup> With respect to smaller impellers, from 3 inches to 26 inches in diameter, Salzman '91 discloses injection molding of plastic with impregnated glass reinforcements.<sup>9</sup> When discussing the use of such mixers, Salzman '91 consistently teaches that such stirrers are useful instead of metallic mixers because of increased strength. For example, Salzman '91 teaches that "[o]n an equal weight basis, structural composites are far stronger than

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<sup>3</sup> Nelles, p. 715, Fig. 2.

<sup>4</sup> Salzman '91 at 39-40.

<sup>5</sup> *Id.* at 39.

<sup>6</sup> *Id.*

<sup>7</sup> *Id.* at 39-40.

<sup>8</sup> *Id.* at 40-41.

<sup>9</sup> *Id.* at 41-42.

the metal alternative . . . ."<sup>10</sup> Salzman '91 also notes that the "principal driving force is cost advantage [including] both initial price and lifetime factors."<sup>11</sup> Salzman '91 also teaches that comparing costs between traditional metal components and reinforced plastic components "must be made based on capital and lifetime operating costs of the entire mixer."<sup>12</sup> The clear implication of Salzman '91 is that the fiber-reinforced mixers are designed to be **replacements for metallic mixers of comparable strength and longevity, not to be discarded after a single use.**

Similar to Salzman '91, Salzman '88 (referenced in Salzman '91) teaches for the use of fiber reinforced plastics when designing stirrer shafts. In addition to teaching that fiber reinforcements are required to provide adequate strength, Salzman '88 goes further, teaching that mere fiber reinforcement is not enough. In particular, materials merely injected with 30% carbon fibers of short length and random fiber orientation provide inadequate tensile strength.<sup>13</sup> To engineer adequate strength into thermoplastics for use as stirring shafts, the fiber reinforcements must be specifically oriented within the shaft.<sup>14</sup> Specifically, Salzman '88 teaches that long shaft lengths are preferred, and these shaft may be "custom-fabricated" on a "computer-controlled filament winder."<sup>15</sup> The reference continues by stressing the importance of achieving "directional strength properties . . . by winding continuous fibers at precise angles . . . to resist the combined torque, thrust, and bending loads of the mixer shaft."<sup>16</sup> These teachings are consistent with Salzman '91, and clearly teach away from the use of non-reinforced plastics in stirrers.

The Strah reference is inapplicable to the present analysis of claim 163. Strah discloses a quick-connect-disconnect fluid line coupler, including a male element 10 received by a female assembly 11 for locking two fluid lines to one another.<sup>17</sup> Strah distinguishes itself from prior art couplers with its (i) effective and durable seal at pressure, (ii) relatively slim body, and (iii)

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<sup>10</sup> *Id.* at 39.

<sup>11</sup> *Id.* at 39 (emphasis added).

<sup>12</sup> *Id.* at 43 (emphasis added).

<sup>13</sup> Salzman '88 at 53.

<sup>14</sup> *Id.* at 53.

<sup>15</sup> Salzman '88 at 52.

<sup>16</sup> *Id.* at 52.

single-handed manipulation.<sup>18</sup> These features are inapplicable to the present claim and will be discussed in detail below with respect to other claims.

Amended claim 163 is allowable because the prior art references, even if combined, do not establish a prima facie case of obviousness. Among other things, "[t]o establish a prima facie case of obviousness, . . . the prior art reference (or references when combined) must teach or suggest all the claim limitations."<sup>19</sup> Here, none of the cited references teaches or suggests all the claim limitations. In particular, none of the references teaches a "a single use plastic stirrer comprising a shaft having a plastic core and a plastic mixing blade on the shaft, . . . said plastic stirrer being removable from [a] coupling after a mixing operation to permit discard and replacement of the stirrer after a single use." In Salzman '88 and '91, developers faced the challenge of creating a stirrer having strength and durability properties similar to those of steel. To overcome these significant challenges, the fiber-reinforced stirrers and stir shafts taught by Salzman '88 and '91 include carefully-designed fiber structures for providing the stirrer with high strength and rigidity. Such stirrers are much more expensive to design and manufacture than the claimed stirrers having a plastic core. The Salzman '88 and '91 stirrers are carefully designed for extended, repeated use. As such, there is no teaching in the newly cited references for a replaceable stirrer designed for only a single use.

In contrast to the challenges faced in Salzman '88 and '91, a key challenge in operating parallel reactors, such as the claimed reactor, is turning the reactor around between experiments. If stirrers must be cleaned between each set of experiments, system efficiency decreases and the potential for contamination increases. Therefore, a single use plastic stirrer comprising a shaft having a plastic core and a plastic mixing blade removable after a mixing operation to permit discard and replacement of the stirrer after a single use overcomes this entirely different challenge. A shaft having a plastic core is of particular importance in the parallel reactor of claim 163 because each plastic stirrer is removable from its coupling after a mixing operation to permit replacement. Plastic core stirrers are less costly to manufacture, are lighter, and may be formed from various plastic materials. Because of their low cost, replaceable plastic core stirrers eliminate the problems associated with cleaning stirrers and possible cross-test contamination.

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<sup>17</sup> Strah, column 1, lines 56-67.

<sup>18</sup> Strah, column 1, lines 31-41.

<sup>19</sup> M.P.E.P. § 706.02(j).

Steel, glass, and fiber-reinforced shafts, which are more expensive and are typically not replaceable, do not offer these advantages.

No combination of cited references teaches these claim features. Again, the newly cited prior art teaches stirrers having the strength and durability of steel for reuse. In contrast, the present claims contemplate incorporating inexpensive, replaceable stirrers, so that the claimed reactor may be quickly turned around and prepared for additional experimentation. None of the other references relied upon in the Office action discloses or suggests the non-obvious combination of features of claim 163.

For at least these reasons, claim 163 is believed to be in condition for allowance. Claims 164-170 and 215-218, which depend directly or indirectly from claim 163, are submitted as patentable for the same reasons as claim 163.

#### **Claim 165**

Reconsideration of the rejection of amended claim 165 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Amended claim 165 defines a parallel reactor wherein the coupling is attached to the upper spindle portion for rotation therewith, and wherein the shaft of the stirrer has a quick-connect/disconnect element thereon adapted for releasable engagement with the coupling and for preventing relative rotation of the coupling and the stirrer. Claim 165 is amended to further emphasize that the structure of the coupling both (i) provides releasable engagement of the stirrer and (ii) prevents relative rotation of the stirrer with respect to the coupling. The cited prior art references fail to teach or suggest these novel features.

In particular, Strah, the reference cited for its “notoriously well known quick-disconnect coupling mechanism,”<sup>20</sup> fails to teach a coupling mechanism that is capable of providing both releasable engagement and rotation prevention of the male element 10 (stirrer) relative the female assembly 11 (coupling).<sup>21</sup> Strah teaches a disconnectable fluid line coupler, but provides no teaching or suggestion that its coupler prevents rotation between the male element and the

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<sup>20</sup> September 25, 2003 Office action, page 3, line 26.

<sup>21</sup> Strah, Fig. 1.

female assembly, as would be required for a coupler for a stir shaft. As such, Strah cannot render amended claim 165 obvious.

In addition, Strah provides no inherent teaching for preventing rotation between the male element and the female assembly. A bore 11d of the female assembly receives a cylindrical portion 10m of the male member when the coupler is assembled.<sup>22</sup> A bushing 17 and an o-ring seal 15 seal the male element within the female assembly, and pins 27 engage a circumferential groove 32 in the male element to limit axial movement of the male element.<sup>23</sup> None of these features limits rotation of the male member with respect to the female assembly, either explicitly or inherently. As such, Strah and the other references of record cannot render claim 165 obvious.

For at least these reasons, claim 165 is believed to be in condition for allowance. Claim 166, which depends directly from claim 165, is submitted as patentable for the same reasons as claim 165.

#### **Claim 169**

Reconsideration of the rejection of claim 169 under 35 U.S.C. §103 as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

As discussed in Applicant's previous Office action response<sup>24</sup>, claim 169 is directed to a parallel reactor having a drive mechanism comprising (i) a gear train for rotating each magnetic feed through device and (ii) a motor for rotating gears of the gear train to effect conjoint rotation of the multi-piece spindles at speeds up to 3000 rpm. None of the references, taken individually or in combination, discloses or suggests these novel elements.

None of the references discloses or suggests a gear train for rotating multiple magnetic feed through devices and a motor for rotating the gear train. In particular, newly applied references Salzman and Strah fail to disclose a gear train or a motor for rotating gears at speeds up to 3000 rpm. As discussed in Applicant's previous response, Salvat discloses a shaft-stirred magnetic feed through device for stirring the contents of a vessel, but it does not disclose

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<sup>22</sup> *Id.* at column 1, lines 68 to 72.

<sup>23</sup> *Id.* at column 1, line 72 to column 2, line 39.

<sup>24</sup> Letter to Patent and Trademark Office, August 5, 2003, page 19.

multiple devices connected by a gear train. Aldrich similarly fails to disclose a common gear train for rotating multiple shafts. Corkan discloses stir bar stirring with a fifteen-vessel solid-state stirring assembly 16A (Fig. 2), but fails to disclose a gear train for rotating each of the stir bars. Nelles discloses a single reactor and therefore has no need for such a gear train. Lebl includes multiple reaction vessels, but fails to disclose magnetic feed through devices for each vessel or a gear train connecting such devices. None of the other references of record provides further relevant teaching. As a result, the cited references do not render claim 169 obvious because they do not show or suggest a gear train. If the Examiner maintains the rejection of the present claim, Applicants request the courtesy of a phone call or a more specific explanation of the present rejection specifically explaining what reference, or group of references, teach these novel features.

For these reasons, claim 169 is believed to be in condition for allowance. Claim 170, which depends directly from claim 169, is submitted as patentable for the same reasons as claim 169.

#### **Claim 171**

Reconsideration of the rejection of claim 171 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.

Amended claim 171 defines plastic stirrers for use in stirring reaction mixtures in a parallel reactor. The reactor comprises vessels for containing the reaction mixtures, metal spindle portions associated with the vessels, couplings on the metal spindle portions for releasably coupling the plastic stirrers to the spindle portions, and a drive system for rotating the metal spindle portions and the plastic stirrers. Importantly, each plastic stirrer comprises a **shaft having a plastic core** and a plastic mixing blade on the shaft. The shaft has a quick-connect/disconnect element thereon adapted for engagement with the coupling for releasably coupling the plastic stirrer to the metal spindle portion for rotation therewith. Upon completion of a mixing operation, the **plastic stirrer is adapted to be disconnected from the coupling, discarded and replaced by a new plastic stirrer after a single use.**

As discussed above with respect to claim 163, Aldrich, Salzman and Strah fail to disclose these novel features. Amended claim 171 is allowable because the prior art references, even



when combined, do not establish a prima facie case of obviousness because they do not teach or suggest all the claim limitations." In particular, none of the references teaches a plastic stirrer designed for a single use comprising a shaft having a plastic core and a plastic mixing blade on the shaft being removable from a coupling after a mixing operation to permit discard and replacement of the stirrer after a single use." As discussed in detail above, the developers in Salzman '88 and '91 faced the challenge of creating a stirrer having the strength and durability of steel. To overcome these significant challenges, the references teach fiber-reinforced stirrers and stir shafts with carefully-designed fiber structures for providing the stirrer with high strength and rigidity. Such stirrers are much more expensive and are carefully designed for extended, repeated use.

In contrast to the challenges faced in Salzman '88 and '91, a key challenge in operating parallel reactors, such as the claimed reactor, is turning the reactor around between experiments. If stirrers must be cleaned between each set of experiments, system efficiency decreases and the potential for contamination increases. Therefore, a single use plastic stirrer comprising a shaft having a plastic core and a plastic mixing blade removable after a mixing operation to permit discard and replacement of the stirrer after a single use overcomes this entirely different challenge.

For at least these reasons, claim 171 is believed to be in condition for allowance. Claims 172-175 and 219-221, which depend directly or indirectly from claim 171, are submitted as patentable for the same reasons as claim 171.

### **Claim 173**

Reconsideration of the rejection of claim 173 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.

Amended claim 173 defines plastic stirrers wherein the quick-connect/disconnect element comprises a **pin on the shaft receivable in a bayonet slot in the coupling**. None of the cited references, in particular Strah, disclose these elements. Strah discloses parallel pins 27 slidably received in sloping slots 28 of the female assembly 11 for engaging a groove 32 on the male

element 10.<sup>25</sup> Unlike claim 173, there is no **pin on the shaft** receivable in a **bayonet slot in the coupling**. In Strah, the pin is received within a slot of the female assembly, or coupler, rather than on the male element, or shaft. Moreover, there is no bayonet slot in the coupling, instead the male element, or shaft, includes a groove. Without teaching or suggesting each and every element of the claim, the Office has failed to meet its burden of establishing a prima facie case of obviousness.

For at least these reasons, claim 173 is believed to be in condition for allowance.

### **Claim 175**

Reconsideration of the rejection of claim 175 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.

Claim 175 further defines the plastic stirrers as sized for reception in a vessel having a volume of less than about 20 ml. None of the cited references disclose plastic stirrers sized for reception in such a vessel. For example, a hypothetical cylindrical vessel having an interior height equal to its interior diameter and a volume of 20 ml yields a vessel with an inside height and inside diameter of 2.94 centimeters (1.16 inches) each. None of the references disclose a plastic stirrer sized for reception in a vessel having an inside diameter of 2.94 centimeters (1.16 inches). For example, Salzman '88 teaches stirrers having much larger diameters, such as 45 inches, 39 inches and 43 inches.<sup>26</sup> Similarly, Salzman '91 teaches stirrers having diameters of 134 inches and within a range of 3 inches to 26 inches.<sup>27</sup> None of these stirrers is small enough to stir a vessel having a capacity of less than about 20 ml. Because none of the references teach a plastic stirrer sized for reception in a vessel having a volume of less than about 20 ml, the Office has failed to meet its burden of establishing a prima facie case of obviousness.

For at least these reasons, claim 175 is believed to be in condition for allowance.

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<sup>25</sup> Strah, column 2, lines 23-46.

<sup>26</sup> Salzman '88, pages 54 and 55.

<sup>27</sup> Salzman '91, page 41.

### Claim 176

Reconsideration of the rejection of claim 176 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claim 176 is directed to an apparatus for the parallel processing of reaction mixtures, comprising

a reactor block having a series of wells therein extending down from an upper surface of the block for containing the reaction mixtures,  
**an upper plate removably secured to said reactor block over said upper surface thereof, said upper plate having openings therein in registry with the wells in the reactor block,**  
**stirring mechanisms attached to said upper plate and removable with the upper plate for stirring said reaction mixtures, said stirring mechanisms extending down through the openings in the upper plate and into respective wells, and**  
seals for sealing against leakage through said upper plate openings when the upper plate is secured to the reactor block,  
each stirring mechanism comprising a drive mounted on said upper plate and a multi-piece spindle rotatable by said drive, said multi-piece spindle having a metal upper spindle portion, **a single use plastic stirrer**, and a coupling for releasably coupling the plastic stirrer to the metal upper spindle portion in a position wherein the stirrer extends down into a respective well, **said plastic stirrer being removable from said coupling after a mixing operation to permit discard and replacement of the stirrer after a single use.**

None of the cited references discloses this unique and patentable array of features. In particular, the apparatus comprises stirring mechanisms attached to an upper plate removably secured over an upper surface of a reactor block and having openings therein in registry with wells of the reactor block for stirring the reaction mixtures. The present rejection of claim 176 relies heavily upon the teaching of Nelles and Lebl.<sup>28</sup> Nelles discloses a single reactor with a rotating shaft and stirring implement.<sup>29</sup> Nelles discloses a lid engaging a pressure container sealing the reactor. Nelles fails to disclose a reactor block with wells, and the lid is not equivalent to the plate defined in claim 176, because it does not include openings therein in registry with multiple wells of a reactor block. Lebl includes multiple reaction vessels 219 threaded into individual valve caps 227 mounted underneath a plate 211 for simultaneously

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<sup>28</sup> September 25, 2003, Office action, page 6, lines 11-13 and July 1, 2003, phone conference with Examiner.

opening or closing the reaction vessels and dispensing solution into an individual reaction vessel by syringe 217.<sup>30</sup> Importantly, Lebl fails to disclose stirring mechanisms of any sort attached to a plate and removable with the plate.

First, combining Nelles and Lebl does not produce the claimed invention. Nelles teaches a single, shaft-stirred vessel, while Lebl teaches multiple vessels sealed simultaneously with a common plate. Applying the stirring capability of Nelles to the multiple vessels of Lebl does not teach one skilled in the art about the advantages of attaching the stirring mechanisms to a common, upper plate. Nelles teaches that stirring a single vessel requires a cap with an opening for sealing and receiving a shaft. Nelles fails to teach one skilled in the art the advantage of combining several of its caps together as a single plate and mounting multiple shafts on the plate for stirring multiple vessels simultaneously. Moreover, Lebl similarly fails to teach any advantage associated with mounting multiple stirring mechanisms on a single plate for stirring several reactions simultaneously.

Nelles and Lebl cannot properly be combined in the manner suggested by the Examiner because they are directed to two different processes having differing requirements. Nelles is directed to a single, two-liter, stirred reactor from which samples may be removed every 10 minutes. Nelles focuses on solving the problems associated with the need for sampling from a reactor at pressure.<sup>31</sup> Nelles does not mention the need for additional parallel reactors or the need for multiple stirring mechanisms for stirring the multiple reactors. In contrast to Nelles, Lebl focuses on a plurality of reactor vessels that may be opened or closed simultaneously via common valving associated with a common plate. Lebl does not require or disclose a need for stirring, especially stirring mechanisms attached to a common plate. Indeed, improperly utilizing Applicants' disclosure and hindsight, combining the Nelles reactor with the Lebl apparatus does provide an advantage over the single vessel apparatus of Nelles and the multiple vessels of limited functionality of Lebl. But there is no teaching or suggestion to combine these references. Simply because their combination appears possible in light of Applicants' disclosure does not mean that there is an adequate teaching for an obviousness rejection.

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<sup>29</sup> Nelles, Fig. 2.

<sup>30</sup> Lebl, Figs. 8A and 8B.

<sup>31</sup> Nelles translation, page 2.

"Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art."<sup>32</sup> Here, there is no motivation to modify Lebl with Nelles because Lebl does not suffer from the drawback Nelles aims to solve, namely, sampling while at pressure (Nelles opens all vessels to atmosphere for sampling); and there is no motivation to modify Nelles with the teaching of Lebl because Nelles is directed to stirring and sampling a single vessel, whereas Lebl is directed to opening and closing multiple vessels simultaneously. The only motivation to combine Lebl and Nelles to produce the claimed invention -- wherein stirring mechanisms are attached to an upper plate removably secured over an upper surface of a reactor block and having openings therein in registry with wells of the reactor block for stirring the reaction mixtures -- is from Applicants' own disclosure.

In addition, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination."<sup>33</sup> It may be possible to combine Nelles and Lebl, but because neither suggests the desirability of the combination, the resultant combination is not obvious. Because there is no teaching in Lebl or Nelles for the combination, one skilled in the art would not be motivated to use the Lebl apparatus with the Nelles reactor. As such, the Office has not met its burden in establishing a prima facie case of obviousness. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 176.

In addition to the foregoing, the stirring mechanisms of claim 176 comprise a drive mounted on the upper plate and a **single use plastic stirrer** releasably coupled to a metal upper spindle portion for **removal after a mixing operation to permit discard and replacement of the stirrer after a single use**. This portion of claim 176 is allowable for the same reasons as set forth above with respect to claim 163. Applicants will not repeat the details of those arguments here.

As a result, the art of record do not render claim 176 obvious. For at least these reasons, claim 176 is believed to be in condition for allowance.

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<sup>32</sup> M.P.E.P. § 2143.01.

**Claim 177**

Reconsideration of the rejection of claim 177 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvet and Aldrich, Salzman or Strah is respectfully requested.

Claim 177 is directed to an apparatus for parallel processing of reaction mixtures comprising

**a reactor block having a series of wells therein** extending from an exterior surface of the block for containing the reaction mixtures,  
**a removable plate removably secured to the reactor block, the removable plate having openings therein in registry with the wells** in the reactor block,  
a temperature control system for regulating the temperature of the reaction mixtures, and  
**a stirring system attached to the removable plate and removable with the removable plate for agitating the reaction mixtures**, the stirring system comprising:  
spindles extending into respective wells, each of the spindles having a first end portion and a second end portion,  
a stirring blade attached to the first end portion of each of the spindles, and  
a drive mechanism located external to the vessels that is adapted to rotate the spindles.

Claim 177 is patentable for many of the same reasons as set forth above with respect to claim 176. In particular, none of the references disclose (i) a reactor block having a series of wells therein, (ii) a removable plate removably secured to the reactor block, the removable plate having openings therein in registry with the wells in the reactor block, and (iii) a stirring system attached to the removable plate and removable with the removable plate for agitating the reaction mixtures.

As discussed above with respect to claim 176, claim 177 is similarly patentable over Nelles and Lebl for at least the following two reasons. First, combining Nelles and Lebl does not produce the claimed invention. Second, Nelles and Lebl cannot properly be combined in the manner suggested by the Examiner because they are directed to two different processes having differing requirements and their combination invokes improper hindsight.

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<sup>33</sup> *Id.* (emphasis added).

For at least these reasons, claim 177 is believed to be in condition for allowance. Claims 207 and 208, which depend directly from claim 177, are submitted as patentable for the same reasons as claim 177.

#### **Claim 179**

Reconsideration of the rejection of claim 179 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvet and Aldrich, Salzman or Strah is respectfully requested.

Claim 179 is directed to a parallel reactor for simultaneously processing a plurality of reaction mixtures comprising single use plastic stirrers (comprising a shaft having a plastic core and a plastic mixing blade on the shaft) removable from a respective upper spindle portion after a mixing operation to permit discard and replacement of the stirrer after a single use. Claim 179 is submitted as patentable for the same reasons as set forth above with respect to claim 163. Claims 180-182 and 222-225, which depend directly or indirectly from claim 179, are submitted as patentable for the same reasons as claim 179.

#### **Claim 181**

Reconsideration of the rejection of claim 181 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvet and Aldrich, Salzman or Strah is respectfully requested.

Claim 181 is directed to a parallel reactor wherein the drive mechanism comprises a gear train for rotating each magnetic feed through device, and a motor for rotating gears of the gear train to effect rotation of the multi-piece spindles at speeds up to 3000 rpm. Claim 181 is submitted as patentable for the same reasons as set forth above with respect to claim 169. Claim 182, which depends directly from claim 181, is submitted as patentable for the same reasons as claim 181.

#### **Claim 183**

Reconsideration of the rejection of claim 183 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvet and Aldrich, Salzman or Strah is respectfully requested.

Claim 183 is directed to a parallel reactor for simultaneously processing a plurality of reaction mixtures comprising single use plastic stirrers (each comprising a shaft having a plastic core and a plastic mixing blade on the shaft), a drive system for moving the stirrers, and a coupling for releasably connecting each stirrer to the drive system, the plastic stirrers being removable from the couplings to permit discard and replacement of the stirrer after a single use. Claim 183 is submitted as patentable for the same reasons as set forth above with respect to claim 163. Claims 184-192, 209, and 226-229, which depend directly or indirectly from claim 183, are submitted as patentable for the same reasons as claim 183.

#### **Claim 186**

Reconsideration of the rejection of claim 186 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claim 186 is directed to a parallel reactor wherein the quick-connect/disconnect element comprises a circumferential groove around the shaft for receiving one or more detents in the coupling. Claim 186 is submitted as patentable for the same reasons as set forth above with respect to claim 166.

#### **Claims 190 and 191**

Reconsideration of the rejection of claims 190 and 191 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claims 190 and 191 each define a parallel reactor wherein the drive mechanism comprises a gear train and a motor for rotating gears of the gear train to effect rotation, or movement, of the stirrers. Claims 190 and 191 are submitted as patentable for the same reasons as set forth above with respect to claim 169.

#### **Claim 193**

Reconsideration of the rejection of claim 193 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.



Amended claim 193 defines plastic stirrers for use in stirring reaction mixtures in a parallel reactor. Each plastic stirrer comprises a shaft having a plastic core and a plastic mixing blade on the shaft. The shaft has a quick-connect/disconnect element thereon adapted for engagement with the coupling for releasably connecting the plastic stirrer to the drive system whereby upon completion of a mixing operation the plastic stirrer is adapted to be disconnected from the coupling, discarded and replaced by a new plastic stirrer after a single use. Claim 193 is submitted as patentable for the same reasons as set forth above with respect to claim 163.

Claims 194-196 and 230-232, which depend directly or indirectly from claim 193, are submitted as patentable for the same reasons as claim 193.

#### **Claim 194**

Reconsideration of the rejection of claim 194 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.

Claim 194 is directed to plastic stirrers wherein the quick-connect/disconnect element comprises a circumferential groove in the shaft adapted for receiving one or more detents in the coupling. Claim 194 is submitted as patentable for the same reasons as set forth above with respect to claim 166.

#### **Claim 196**

Reconsideration of the rejection of claim 196 under 35 U.S.C. §103(a) as being unpatentable over Aldrich in view of Salzman, and optionally in view of Strah, is respectfully requested.

Claim 196 is directed to plastic stirrers sized for reception in vessels having volumes of less than 20 ml. Claim 196 is submitted as patentable for the same reasons as set forth above with respect to claim 175.

#### **Claim 197**

Reconsideration of the rejection of claim 197 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claim 197 is directed to a combinatorial chemistry reactor system for parallel processing of reaction mixtures comprising

- a reactor block having a series of wells therein for holding said reaction mixtures,
- a removable plate removably secured to the reactor block, the removable plate **having openings therein in registry with the wells in the reactor block, seals for sealing the wells of the reactor block to allow said reaction mixtures to react under pressure when the removable plate is secured to the reactor block, and**
- a stirring system supported by the removable plate and removable with the removable plate for agitating the reaction mixtures, the stirring system comprising
  - stirrers extending into respective wells, and
  - a drive mechanism located external to the wells for moving the stirrers to agitate reaction mixtures in the wells.

None of the cited references discloses this unique and patentable array of features. In particular, the claimed combinatorial chemistry reactor system comprises a stirring system **supported by and removable with the removable plate, and openings in the removable plate in registry with the wells.** The reactor system further comprises **seals for sealing the wells of the reactor block to allow the reaction mixtures to react under pressure when the removable plate is secured to the reactor block.** The present rejection of claim 197 relies heavily upon the teaching of Nelles and Lebl, as discussed above with respect to claim 176. Nelles discloses a single reactor with a rotating shaft and stirring implement. Nelles fails to disclose a reactor block with wells, and the lid is not equivalent to the plate defined in claim 197, because it does not include openings therein in registry with multiple wells of a reactor block. Lebl includes multiple reaction vessels 219 threaded into individual valve caps 227 mounted underneath a plate 211 for simultaneously opening or closing the reaction vessels and dispensing solution into an individual reaction chamber by syringe 217.<sup>34</sup> Importantly, the Lebl embodiment of Figs. 8 and 8A fails to disclose stirring mechanisms of any sort attached to a plate and removable with the plate. This Lebl embodiment also fails to disclose seals for sealing the vessels with the plate engaging the vessels. In fact, Lebl teaches away from sealing this embodiment when teaching of another embodiment that includes sealing "adapted to resist

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<sup>34</sup> Lebl, Figs. 8A and 8B.

greater internal pressure in a reaction vessel."<sup>35</sup> By teaching greater internal pressures with respect to another embodiment, Lebl teaches away from such elevated pressures in the embodiment of interest in Figs. 8 and 8A.

First, as discussed above with respect to claim 176, combining Nelles and Lebl does not produce the claimed invention. Nelles fails to teach one skilled in the art the advantage of combining several of its caps together as a single plate and mounting multiple shafts on the plate for stirring multiple vessels simultaneously. Moreover, Lebl similarly fails to teach any advantage associated with mounting multiple stirring mechanisms on a single plate for stirring several reactions simultaneously.

The combination of Nelles and Lebl in the manner suggested by the Examiner is improper because the references are directed to two different processes having differing requirements. Nelles focuses on solving the problems associated with the need for sampling from a reactor at pressure. In contrast to Nelles, Lebl focuses on a plurality of reactor vessels that may be opened or closed simultaneously via common valving associated with a common plate. Lebl does not require or disclose a need for multiple stirring mechanisms attached to a common plate. Indeed, improperly utilizing Applicants' disclosure and hindsight, combining the Nelles reactor with the Lebl apparatus does provide an advantage over the single vessel apparatus of Nelles and the multiple vessels of limited functionality of Lebl. However, there is no teaching or suggestion to combine these references. Simply because their combination appears possible in light of Applicants' disclosure does not mean that there is an adequate teaching for an obviousness rejection.

Here, there is no motivation to modify Lebl with Nelles because Lebl does not suffer from the drawback Nelles aims to solve, namely, sampling while at pressure (Nelles opens all the vessels to the atmosphere and then samples); and there is no motivation to modify Nelles with the teaching of Lebl because Nelles is directed to stirring and sampling a single vessel, whereas Lebl is directed to opening and closing multiple vessels simultaneously. The only motivation to combine Lebl and Nelles to produce the claimed invention is from Applicants' own disclosure. It may be possible to combine Nelles and Lebl, but because neither suggests the desirability of the combination, the resultant combination is not obvious. Because there is no teaching in Lebl

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<sup>35</sup> Lebl, column 25, line 23 to column 26, line 12.

or Nelles for the combination, one skilled in the art would not be motivated to use the Lebl apparatus with the Nelles reactor. As such, the Office has not met its burden in establishing a prima facie case of obviousness.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 197. Claims 198-205, which depend directly or indirectly from claim 197, are submitted as patentable for the same reasons as claim 197.

#### **Claim 198**

Reconsideration of the rejection of claim 198 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvet and Aldrich, Salzman or Strah is respectfully requested.

Claim 198 is directed to a system wherein the drive mechanism comprises a **drive train** for driving the stirrers, and a **motor** for driving the drive train. None of the references, taken individually or in combination, discloses or suggests these novel elements.

None of the previously cited references discloses or suggests a drive train for driving the stirrers and a motor for driving the drive train. As discussed in Applicant's previous response, Salvet discloses a shaft-stirred magnetic feed through device for stirring the contents of a vessel, but it does not disclose a drive mechanism comprising a drive train for moving the stirrers in the wells. Aldrich similarly fails to disclose multiple vessels having a drive mechanism comprising a drive train. Corkan discloses stir bar stirring with a fifteen-vessel solid-state stirring assembly 16A (Fig. 2), but fails to disclose a drive train for moving each of the stir bars. Nelles discloses a single reactor and therefore has no need for such a drive train. Lebl includes multiple reaction vessels, but fails to disclose a drive train for driving stirrers in respective vessels. With respect to the newly cited art, they too fail to provide further relevant teaching. Salzman discloses singular stir shafts, providing no teaching for a drive train for driving multiple stirrers. Strah has no relevance to the pending claim, as it simply discloses a fluid line coupler.

As a result, the cited references do not render claim 198 obvious because they do not show or suggest a drive train and a motor for driving the drive train. For these reasons, claim 198 is believed to be in condition for allowance. If the Examiner maintains the rejection of the present claim, Applicants request the courtesy of a phone call or a more specific explanation of

the present rejection specifically explaining what reference, or group of references, teach these novel features.

Claim 199, which depends directly from claim 198, is submitted as patentable for the same reasons as claim 198.

#### **Claim 199**

Reconsideration of the rejection of claim 199 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claim 199 is directed to a system wherein the drive train comprises **a plurality of drive gears in mesh with one another** and a **motor** for driving the drive gears. None of the references, taken individually or in combination, discloses or suggests these novel elements.

As discussed above with respect to claim 198, none of the references discloses a drive train. In addition, none of the references discloses or suggests a drive train comprising **a plurality of drive gears in mesh with one another**. Salvat discloses a shaft-stirred magnetic feed through device, but discloses no meshing gears. Aldrich and Salzman disclose motor-turned shafts, but disclose no meshing gears. Corkan teaches stir bar stirring, but discloses no meshing gears. Nelles discloses stirring, but discloses no meshing gears. Lebl includes multiple reaction vessels, but discloses no meshing gears. Strah is immaterial to this claim. As a result, the cited references do not render claim 199 obvious because they do not show or suggest a plurality of drive gears in mesh with one another. For at least these reasons, claim 199 is believed to be in condition for allowance. If the Examiner maintains the rejection of the present claim, Applicants request the courtesy of a phone call or a more specific explanation of the present rejection specifically explaining what reference, or group of references, teach these novel features.

#### **Claim 200**

Reconsideration of the rejection of claim 200 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvat and Aldrich, Salzman or Strah is respectfully requested.

Claim 200 is directed to a system wherein the drive mechanism comprises a **plurality of drive gears on the stirrers**, and **one or more motors** for driving the drive gears. As discussed above with respect to claim 199, none of the references discloses or suggests drive gears. In addition, none of the references discloses or suggests a plurality of **drive gears on the stirrers**, and one or more motors for driving the drive gears. Salvetti discloses a shaft-stirred magnetic feed through device, but discloses no drive gears on the stirrers. Aldrich and Salzman disclose motor-turned shafts, but disclose no drive gears on the stirrers. Corkan teaches stir bar stirring, but discloses no drive gears on the stirrers. Nelles discloses stirring, but discloses no drive gears on the stirrers. Lebl includes multiple reaction vessels, but discloses no drive gears on the stirrers. Strah is immaterial to this claim. As a result, the cited references do not render claim 200 obvious because they fail to show or suggest a plurality of drive gears on the stirrers.

For at least these reasons, claim 200 is believed to be in condition for allowance. Claim 201, which depends directly from claim 200, is submitted as patentable for the same reasons as claim 200.

#### **Claim 206**

Reconsideration of the rejection of claim 206 under 35 U.S.C. §103(a) as being unpatentable over Nelles in view of Lebl, Corkan, Salvetti and Aldrich, Salzman or Strah is respectfully requested.

Claim 206 is directed to a combinatorial chemistry reactor system for parallel processing of reaction mixtures comprising

- a reactor block having a series of wells therein extending down from an upper surface of the block, said wells holding said reaction mixtures,
- an upper plate removably secured to the reactor block in face-to-face relation with said upper surface**, the removable plate having openings therein in registry with the wells in the reactor block,
- seals for sealing the wells of the reactor block to allow said reaction mixtures to react under pressure** when the removable plate is secured to the reactor block, and
- a stirring system supported by the removable plate and removable with the removable plate** for agitating the reaction mixtures, the stirring system comprising
  - stirrers extending into respective wells, and
  - a drive mechanism located external to the wells for moving the stirrers to agitate reaction mixtures in the wells, said drive mechanism comprising a **drive**

**train for driving said stirrers** and one or more motors for driving said drive train, said stirrers being removably attached to said drive mechanism.

Claim 206 is directed to several features previously discussed with respect to other claims noted above. In particular, none of the references of record discloses an upper plate removably secured to the reactor block in face-to-face relation with the upper surface of the reactor block. Please refer to the discussion of claim 176 above. Moreover, none of the references discloses seals for sealing the wells of the reactor block to allow the reaction mixtures to react under pressure when the removable plate is secured to the reactor block, as discussed above with respect to claim 197. Similarly, none of the references discloses a stirring system supported by the removable plate and removable with the removable plate, as discussed above with respect to claim 176. Finally, none of the references discloses a drive train for driving the stirrers, as discussed above with respect to claim 198.

For at least these reasons, claim 206 is believed to be in condition for allowance.

#### **New Claims**

New claims 211, 213, 216, 219, 223, 227, and 230 are added herein and are submitted as patentable over the cited prior art. In particular, these claims each include the feature of a plastic stirrer comprising a shaft having a plastic core consisting of plastic. Applicants submit that such claims are patentable over the art of record, as none of the cited references teach a shaft having a plastic core consisting of plastic. Some stirrers in the cited art may comprise plastic, but they are also comprised of other materials, such that they do not render these claims unpatentable. Early allowance of these claims is respectfully requested.

New claims 212, 214, 217, 220, 224, 228, and 231 are added herein and are also submitted as patentable over the cited prior art. In particular, these claims each include the feature of a plastic stirrer comprising a shaft having a plastic core consisting of polyethylethylketone (PEEK). Applicants submit that such claims are patentable over the art of record, as none of the cited references teach a stirrer shaft having a plastic core consisting of polyethylethylketone (PEEK). Early allowance of these claims is respectfully requested.

New claims 218, 221, 225, 229, and 232 are added herein and are also submitted as patentable over the cited prior art. In particular, these claims each include the feature of a plastic stirrer comprising a shaft having a plastic core consisting of polytetrafluoroethylene (PTFE).

Applicants submit that such claims are patentable over the art of record, as none of the cited references teach a stirrer shaft having a plastic core consisting of polytetrafluoroethylene (PTFE). Early allowance of these claims is respectfully requested.

New claims 215, 222, and 226 are added herein and are submitted as patentable over the cited prior art. In particular, these claims each include the feature of each vessel sealed against fluid communication with the other vessels. Applicants submit that such claims are patentable over the art of record, as none of the cited references teach vessels sealed against communication with one another in combination with the other patentable features of the claims from which these claims depend. Early allowance of these claims is respectfully requested.

New claims 233 and 234 are added herein and are submitted as patentable over the cited prior art. In particular, these claims each disclose a method of making and characterizing materials within a parallel reactor apparatus by, among other things, simultaneously stirring reaction mixtures, removing a plurality of plastic stirrers after the stirring, and discarding the plurality of plastic stirrers after a single use. Applicants submit that such claims are patentable over the art of record, as none of the cited references teach such a method. Early allowance of these claims is respectfully requested.



**Conclusion**

The Commissioner is hereby authorized to charge the amount of \$1,218.00 to Deposit Account No. 19-1345 (\$618.00 for the additional claim fee; \$420.00 for a two-month extension of time; and \$180.00 to cover the fee specified in 37 CFR §1.17(p) for submission of this Supplemental Information Disclosure Statement). The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

In view of the foregoing, favorable reconsideration and allowance of this application is requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'BPK', with a stylized flourish at the end.

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